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#### (54) Title: FLUOROCOMBRETASTATIN AND DERIVATIVES THEREOF

ST2303

synthesis of difluorocombretastatin

BOURDO
CHAP

H

CFBs

Te-130°C

CHAP

TE-178°C

TEOMSO
CHAP

Te-100°C syn

Te-100°C syn

Tokens(reflux)

TOKENSO
CHAP

(57) Abstract: The present invention is related to new derivatives of Combretastatin, of Formula (I) obtained by total synthesis. The strategy developed for each of the compounds is to i) replace a halogen (i.e. fluorine atom) to hydrogen on olefinic bound; ii) replace an aromatic ring in a natural product with an amino-aromatic ring. Said compounds recognize and bind the tubulin site: are useful for treating pathological states which arise from or are exacerbated by cell proliferation - as anticancer and/or antiangiogenic activity, in a mammal - to pharmaceutical compositions comprising these compounds.



GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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